COURTESY COPY OF PENDING CLAIMS

1. A method of making a recombinant nucleic acid, the method comprising:

providing a plurality of parental character strings corresponding to a plurality of nucleic acids, which character strings, when aligned for maximum identity, comprise at least one region of heterology;

aligning the character strings;

defining a set of character string subsequences, which set of subsequences comprises subsequences of at least two of the plurality of parental character strings;

providing a set of oligonucleotides corresponding to the set of character string subsequences;

annealing the set of oligonucleotides; and,

elongating one or more members of the set of oligonucleotides with a polymerase, or ligating at least two members of the set of oligonucleotides with a ligase, thereby producing one or more recombinant nucleic acid.

2. The method of claim 1, wherein the character strings, when aligned for maximum identity comprise at least one region of similarity.

3. The method of claim 1, wherein at least one of the parental character strings is an evolutionary or artificial intermediate.

4. The method of claim 1, wherein at least one of the parental character strings corresponds to a designed nucleic acid.

5. The method of claim 4, wherein the designed nucleic acid represents an energy minimized design for an encoded polypeptide.

6. The method of claim 1, further comprising applying one or more genetic operator to one or more of the parental character strings, or to one or more of the character string subsequences, wherein the genetic operator is selected from: a mutation of the one or more parental character strings or one or more character string subsequences, a multiplication of the one or more parental character strings or one or more character string subsequences, a fragmentation of the one or more parental character strings or one or more character string subsequences, a crossover between any of the one or more parental character strings or one or more character string subsequences or an additional character string, a ligation of the one or more parental character strings or one or more character string subsequences, an elitism calculation, a calculation of sequence homology or sequence similarity of aligned strings, a recursive use of one or more genetic operator for evolution of character strings, application of a randomness operator to the one or more parental character strings or the one or more character string subsequences, a deletion mutation of the one or more parental character strings or one or more character string subsequences, an insertion mutation into the one or more parental character strings or one or more of character string subsequences, subtraction of the of the one or more parental character strings or one or more character string subsequences with an inactive sequence, selection of the of the one or more parental character strings or one or more character string subsequences with an active sequence, and death of the one or more parental character strings or one or more of character string subsequences.

7. The method of claim 1, further comprising selecting a diplomat sequence, which diplomat sequence comprises an intermediate level of sequence similarity between two or more of the plurality of character strings.

8. The method of claim 1, further comprising selecting cross-over sites and corresponding bridging oligonucleotides to facilitate recombination between the two or more parental nucleic acids.

9.   (AMENDED). The method of claim 8, wherein the two or more parental character strings display low sequence similarity.

10. **(AMENDED).** The method of claim 8, further comprising determining a sequence for one or more putative recombinant nucleic acids resulting from in silico recombination of the two or more parental character strings at the cross-over sites, and performing one or more in silico simulation of activity for one or more of the putative recombinant nucleic acids or for a protein encoded by one or more of the putative recombinant nucleic acids.

11. The method of claim 10, further comprising synthesizing the putative recombinant nucleic acid by providing fragments of the two or more parental nucleic acids and at least one of the corresponding bridge oligonucleotides, hybridizing the fragments and the bridge oligonucleotides and elongating the hybridized fragments with a polymerase or a ligase.

12. The method of claim 1, wherein the set of oligonucleotides comprise a plurality of overlapping oligonucleotides.

13. The method of claim 1, wherein the set of character string subsequences is defined by selecting a length for the character string and subdividing at least two of the plurality of parental character strings into segments of the selected length.

14. The method of claim 1, wherein aligning the character strings is performed in a digital computer or in a web-based system.

15. The method of claim 1, further comprising synthesizing a set of single-stranded oligonucleotides which correspond to the set of character string subsequences, thereby providing the set of oligonucleotides.

16. The method of claim 1, further comprising:
pooling all or part of the set of oligonucleotides;
hybridizing the resulting pooled oligonucleotides; and,

extending a plurality of the resulting hybridized oligonucleotides, wherein at least one of the resulting extended double stranded nucleic acids comprises sequences from at least two of the plurality of parental character strings.

17. The method of claim 15, further comprising denaturing the double stranded nucleic acids, thereby producing a heterogeneous mixture of single-stranded nucleic acids.

18. The method of claim 15, further comprising:

(i) denaturing the double stranded nucleic acids, thereby producing a heterogeneous mixture of single-stranded nucleic acids;

(ii) re-hybridizing the heterogeneous mixture of single-stranded nucleic acids; and

(iii) extending the resulting rehybridized double stranded nucleic acids with a polymerase.

19. The method of claim 17, further comprising repeating steps (i) (ii) and (iii) at least twice.

20. The method of claim 1, further comprising selecting the one or more recombinant nucleic acid for a desired property.

21. **(AMENDED).** The method of claim 1, wherein the set of oligonucleotides is provided by synthesizing the oligonucleotides to comprise one or more modified parental character string subsequence, which subsequence comprises one or more of:

a parental character string subsequence modified by one or more replacement of one or more character of the parental character string subsequence with one or more different character;

a parental character string subsequence modified by one or more deletion or insertion of one or more characters of the parental character string subsequence;

a parental character string subsequence modified by inclusion of a degenerate sequence character at one or more randomly or non-randomly selected positions;

a parental character string subsequence modified by inclusion of a character string from a different character string from a second parental character string subsequence at one or more position;

a parental character string subsequence which is biased based upon its frequency in a selected library of nucleic acids; and,

a parental character string subsequence which comprises, or encodes a polypeptide that comprises, one or more sequence motif, which sequence motif is artificially included in the subsequence.

22. The method of claim 21, wherein the sequence motif comprises an N-linked glycosylation sequence, an O-linked glycosylation sequence, a protease sensitive sequence, a collagenase sensitive sequence, a Rho-dependent transcriptional termination sequence, an RNA secondary structure sequence that affects the efficiency of transcription, an RNA secondary structure sequence that affects the efficiency of translation, a transcriptional enhancer sequence, a transcriptional promoter sequence, or a transcriptional silencing sequence.

23. The method of claim 1, wherein the oligonucleotide set contains one or more altered or degenerate positions as compared to the corresponding subsequence of one or more parental character string.

24. The method of claim 1, further comprising selecting the one or more recombinant nucleic acid based upon its hybridization to a selected nucleic acid or to a set of selected nucleic acids.

25. **(AMENDED).** The method of claim 1, wherein the plurality of parental character strings comprises at least two parental character strings, wherein the oligonucleotide set comprises at least one oligonucleotide member comprising a chimeric nucleic acid sequence that comprises a subsequence from each of at least two parental

character strings, wherein the subsequences from each parental character string are separated by a crossover point.

26. **(AMENDED).** The method of claim 25, wherein the crossover point is selected by aligning at least one substring of each of at least two of the parental character strings to display pairwise identity between the substrings, and selecting a point within the aligned sequence as the crossover point.

27. The method of claim 25, wherein the crossover point is selected randomly.

28. The method of claim 25, wherein the crossover point is selected non randomly.

29. The method of claim 25, wherein the crossover point is selected non randomly by selecting a crossover point approximately in the middle of one or more identified pairwise identity region.

30. The method of claim 25, wherein at least one crossover point for at least one oligonucleotide member is selected from a region outside of an identified pairwise homology region.

31. The method of claim 1, further comprising adding one or more oligonucleotide member of the set of oligonucleotides at a concentration which is higher than at least one or more additional oligonucleotide member of the set of oligonucleotides.

32. The method of claim 1, further comprising incubating one or more member of the oligonucleotide set with the recombinant nucleic acid and a polymerase.

33. The method of claim 1, further comprising denaturing the recombinant nucleic acid, and contacting the recombinant nucleic acid with at least one additional nucleic acid from the oligonucleotide set.

34. (AMENDED). The method of claim 1, further comprising denaturing the recombinant nucleic acid, and contacting the recombinant nucleic acid with at least one additional nucleic acid produced by cleavage of at least one parental nucleic acid.

35. (AMENDED). The method of claim 1, further comprising denaturing the recombinant nucleic acid, and contacting the recombinant nucleic acid with at least one additional nucleic acid produced by cleavage of a parental nucleic acid, which parental nucleic acid is cleaved by one or more of: chemical cleavage, cleavage with a DNAse, and cleavage with a restriction endonuclease.

36. (AMENDED). The method of claim 1, wherein at least one parental nucleic acid encodes one or more or proteins selected from: EPO, insulin, a peptide hormone, a cytokine, epidermal growth factor, fibroblast growth factor, hepatocyte growth factor, insulin-like growth factor, an interferon, an interleukins, a keratinocyte growth factor, a leukemia inhibitory factor, oncostatin M, PD-ECSF, PDGF, pleiotropin, SCF, c-kit ligand, VEGF, G-CSF, an oncogene product, a tumor suppressor, a steroid hormone receptor, a plant hormone, a disease resistance gene, an herbicide resistance gene product, a bacterial gene product, a monooxygenase, a protease, a nuclease, and a lipase.

37. The method of claim 1, wherein the set of oligonucleotides comprises one or more oligonucleotide member between about 20 and about 60 nucleotides in length.

38. The method of claim 1, further comprising selecting the recombinant nucleic acid for a desired trait or property, thereby providing a selected recombinant nucleic acid.

39. The method of claim 38. further comprising recombining the selected recombinant nucleic acid with one or more of: a homolgous nucleic acid. and an oligonucleotide member from the set of oligonucleotides.

40. The method of claim 1, further comprising selecting the recombinant nucleic acid for a desired trait or property. thereby providing a selected recombinant nucleic acid. wherein the desired trait or property is selected in an in vivo selection assay or a parallel solid phase assay.

41. The method of claim 1, further comprising selecting the recombinant nucleic acid for a desired trait or property, thereby providing a selected recombinant nucleic acid, wherein the desired trait or property is selected in an in vitro selection assay.

42. The method of claim 1, further comprising deconvolution of the recombinant nucleic acid.

43. The method of claim 1, further comprising sequencing or cloning the recombinant nucleic acid.

44. The method of claim 1, wherein the recombinant nucleic acid is synthesized in vitro by assembly PCR.

45. The method of claim 1, wherein the recombinant nucleic acid is synthesized in vitro by error-prone assembly PCR.

46. The method of claim 1, wherein the parental character strings, or oligonucleotide sets are selected in a computer.

47-92 are withdrawn

93.   (AMENDED). A method of producing recombinant nucleic acids, the method comprising:

providing sequences of two or more parental nucleic acids;

selecting cross-over sites for recombination between the sequences of the two or more parental nucleic acids, thereby defining sequences of one or more recombinant nucleic acids that result from a cross-over between at least two of the sequences of the parental nucleic acids;

selecting a sequence of at least one recombinant nucleic acid *in silico* for one or more expected activity; and,

synthesizing a recombinant nucleic acid corresponding to one or more of the selected recombinant sequence.

94. The method of claim 93, further comprising selecting bridging oligonucleotides which correspond to the cross-over sites.

95. **(AMENDED).** The method of claim 94, wherein synthesizing the recombinant nucleic acid comprises providing fragments of two or more of the parental nucleic acids and at least one of corresponding bridge oligonucleotides, hybridizing the fragments and the bridge oligonucleotides and elongating the hybridized fragments with a polymerase or a ligase.

96. **(AMENDED).** The method of claim 93, wherein the sequences of the two or more parental nucleic acids display low sequence similarity.

97. **(AMENDED).** The method of claim 93, wherein selecting the sequence of at least one recombinant nucleic acid in silico comprises one or more of:

(i) performing an energy minimization analysis of a protein encoded by the selected recombinant sequence;

(ii) performing a stability analysis of at least one protein encoded by the selected recombinant sequence;

(iii) comparing an energy minimized model of at least one protein encoded by the selected recombinant sequence to an energy minimized model of a protein encoded by one or more of the parental nucleic acids;

(iv) performing protein threading on one or more protein encoded by the selected recombinant sequence, or a protein encoded by one or more of the parental nucleic acids; and,

(v) selecting the cross-over sites for recombination between the sequences of two or more parental nucleic acids to occur within regions of structural overlap;

(vi) performing one or more of: PDA, a branch-and-terminate combinatorial optimization analysis, a dead end elimination, a genetic or mean-field analysis, or an analysis of protein folding by threading, of the selected recombinant sequence or of a protein encoded by the selected recombinant sequence;

(vii) performing PDA of at least one protein encoded by at least one of the parental nucleic acids; or

comparing a PDA model of a protein encoded by the selected recombinant sequence to a PDA model of a protein encoded by at least one of the two or more parental nucleic acids.

98. The method of claim 93, wherein the step of selecting cross-over sites for recombination between the two or more parental nucleic acid sequences and the step of selecting the at least one recombinant sequence in silico are performed simultaneously.